United States District Court
Northern District of California

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

PLEXXIKON INC.,

Plaintiff,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Defendant.

Case No. 17-cv-04405-HSG

ORDER GRANTING IN PART AND DENYING IN PART MOTION TO EXCLUDE THE EXPERT TESTIMONY OF SUSANA ORTIZ-URDA

Re: Dkt. No. 204

Pending before the Court is Defendant Novartis Pharmaceuticals Corporation's motion to exclude the testimony of Plaintiff Plexxikon Inc.'s expert Susana Ortiz-Urda. Dkt. No. 204. The Court heard argument on this motion on November 1, 2019. *See* Dkt. No. 341. As detailed below, the Court **GRANTS IN PART** and **DENIES IN PART** the motion.

I. BACKGROUND

Defendant challenges the testimony of Plaintiff's clinical expert, Dr. Susana Ortiz-Urda, as speculative and not based on any reliable methodology. Dkt. No. 204. In her expert report, Dr. Ortiz-Urda offers opinions about the treatment of melanoma, its evolution, and how physicians would respond in the hypothetical scenario in which Defendant's drug Tafinlar was not available as a combination therapy with Mekinist. *See* Dkt. No. 227-2 ("Ortiz-Urda Report").

Dr. Ortiz-Urda explains that both immunotherapies and targeted therapies are widely prescribed for the treatment of metastatic melanoma. *See id.* at ¶ 57. However, she explains that there are some circumstances in which targeted therapies are more appropriate for certain $BRAF^{V600E}$ metastatic melanoma patients. *See id.* at ¶¶ 57–62. There are only a few such targeted therapies currently available. *See id.* at ¶ 62. The combination of Tafinlar and Mekinist became the first combination therapy to be approved for the treatment of metastatic melanoma in

January 2014. *See id.* at ¶ 43. In November 2015, Plaintiff's Zelboraf drug was approved by the Food and Drug Administration ("FDA") in combination with Cotellic. *See id.* at ¶ 48. The FDA then approved a third combination therapy, Braftvoi and Mektovi, in June 2018. *Id.* at ¶ 50. Dr. Ortiz-Urda states that these combination therapies, as opposed to monotherapies, have become the standard of care for patients with metastatic melanoma. *Id.* at ¶ 51. She clarifies that in her experience, physicians often prescribe the Tafinlar-Mekinist combination therapy because they are more familiar with it as the first to market, but not because it "is superior from a therapeutic perspective" to the other combination therapies. *Id.* at ¶ 63. In a single paragraph, Dr. Ortiz-Urda also notes that the Tafinlar–Mekinist combination therapy is approved for the treatment of certain other cancers for which the Zelboraf–Cotellic combination is not approved. *See id.* at ¶ 72.

Dr. Ortiz-Urda then offers two primary opinions regarding a hypothetical world in which the Taflinar-Mekinist combination was not an option for treating physicians: (1) $BRAF^{V600E}$ metastatic melanoma patients who were prescribed the combination therapy of Tafinlar and Mekinist would be prescribed another targeted therapy, including Plaintiff's Zelboraf drug in combination with Cotellic; and (2) also that "some percentage of prescribing physicians would prescribe the Zelboraf–Cotellic combination off label to patients for indications for which Tafinlar–Mekinist is approved but the Zelboraf–Cotellic combination is not." *Id.* at ¶ 6(a)–(b); *see also id.* at ¶¶ 66–68, 72. In particular, in addition to metastatic melanoma, Dr. Ortiz-Urda notes that the Tafinlar–Mekinist combination is approved by the FDA for the treatment of non-small cell lung cancer and metastatic anaplastic thyroid cancer. *Id.* at ¶ 72. Although the Zelboraf–Cotellic combination is not approved for the treatment of these cancers, Dr. Ortiz-Urda opines that "physicians would reasonably conclude" that it would be effective against them and prescribe them anyway as they have a similar "mechanism of action" to the Tafinlar–Mekinist combination. *See id.* Dr. Ortiz-Urda repeated similar opinions in her reply report. *See* Dkt. No. 227-4, Ex. 3 ("Ortiz-Urda Reply Report").

II. LEGAL STANDARD

Federal Rule of Evidence 702 allows a qualified expert to testify "in the form of an opinion or otherwise" where:

> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. Expert testimony is admissible under Rule 702 if it is both relevant and reliable. *See Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993). "[R]elevance means that the evidence will assist the trier of fact to understand or determine a fact in issue." *Cooper v. Brown*, 510 F.3d 870, 942 (9th Cir. 2007); *see also Primiano v. Cook*, 598 F.3d 558, 564 (9th Cir. 2010) ("The requirement that the opinion testimony assist the trier of fact goes primarily to relevance.") (quotation omitted).[1] Under the reliability requirement, the expert testimony must "ha[ve] a reliable basis in the knowledge and experience of the relevant discipline." *Primiano*, 598 F.3d at 565. To ensure reliability, the Court "assess[es] the [expert's] reasoning or methodology, using as appropriate such criteria as testability, publication in peer reviewed literature, and general acceptance." *Id.* at 564.

III. DISCUSSION

Defendant contends that as a dermatologist and melanoma specialist at the University of California at San Francisco ("UCSF") Melanoma Center, Dr. Ortiz-Urda is unaware of the behavior of prescribing physicians outside of her own practice group at UCSF. *See* Dkt. No. 204 at 7–9. Defendant thus seeks to preclude her testimony about how physicians outside UCSF would respond in the hypothetical world in which Tafinlar and Mekinist were not available. *Id.* The Court addresses Defendant's argument as it pertains to each of Dr. Ortiz-Urda's opinions about prescription practices for: (1) metastatic melanoma; and (2) other cancers.

A. Prescription Practices for Metastatic Melanoma

First, Dr. Ortiz-Urda opines that if Tafinlar and Mekinist were not available, metastatic melanoma patients who were prescribed this combination therapy would be prescribed another

[1] Whether to admit expert testimony is evaluated "under the law of the regional circuit," so in this case, under the law of the Ninth Circuit. *See Micro Chem., Inc. v. Lextron, Inc.*, 317 F.3d 1387, 1391 (Fed. Cir. 2003).

targeted therapy. *See* Ortiz-Urda Report at ¶¶ 57–62.

Defendant does not argue that Dr. Ortiz-Urda is unqualified to offer opinions about the treatment of melanoma. Rather, Defendant contends that her opinions about what physicians would do without Tafinlar and Mekinist are wholly speculative because during her deposition, Dr Ortiz-Urda acknowledged that she is "less familiar" with the prescribing practices of physicians outside of UCSF. *See id.* at 7 (citing Dkt. No. 204-4, Ex. 3 ("Ortiz-Urda Depo.") at 51:3–52:5; 150:17–151:12). She also explained that prescribing practices may differ based on physicians' perception of side effects and their own clinical experiences. *See id.* (citing Ortiz-Urda Depo. at 31:19–25; 42:24–43:12; 90:13–19). Defendant also points out that Dr. Ortiz-Urda did not engage in any systematic analysis outside her own firsthand experience to obtain information about other physicians' practices. *See id.* at 5, 7–8.

The Court is not persuaded that these statements from Dr. Ortiz-Urda's deposition taken together render her opinions speculative and unreliable. Neither *Daubert* nor Rule 702 requires experts to conduct 50-state surveys before they may offer opinions about the standard of care. Rather, the Supreme Court has cautioned that the *Daubert* inquiry is intended to be flexible, and when evaluating specialized or technical expert opinion testimony, "the relevant reliability concerns may focus upon personal knowledge or experience." *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 150 (1999). The Ninth Circuit has recognized that this is particularly true in the medical context:

> Despite the importance of evidence-based medicine, much of medical decision-making relies on judgment—a process that is difficult to quantify or even to assess qualitatively. Especially when a relevant experience base is unavailable, physicians must use their knowledge and experience as a basis for weighing known factors along with the inevitable uncertainties to mak[e] a sound judgment.

Primiano, 598 F.3d at 565 (quotations omitted).

Here, Dr. Ortiz-Urda's opinions about what metastatic melanoma patients would be prescribed without Tafinlar and Mekinist is based on her "more than ten years of clinical experience treating patients for melanoma," including with the use of targeted therapies such as

Zelboraf, Cotellic, Tafinlar, and Mekinist, and other immunooncology drugs.[2] *See* Ortiz-Urda Report at ¶ 1. She also helped create a multidisciplinary melanoma program at UCSF, in which she incorporated her research and clinical experience. *See id.* at ¶ 3. Dr. Ortiz-Urda's expert report acknowledges that no head-to-head studies have been done comparing Zelboraf to Tafinlar as monotherapies, or comparing the Tafinlar–Mekinist combination with the Zelboraf–Cotellic combination. *See id.* at ¶ 63. Nevertheless, she cites documents and studies about the relative efficacy and side effects of the available treatments. *See id.* at ¶¶ 43, 47–51, 63–68. She explains that in her experience physicians prescribe Tafinlar–Mekinist with more frequency than the other combination therapies because it was the first to market, rather than because of a distinction in its therapeutic benefits. *See id.* at ¶ 63. Dr. Ortiz-Urda also explains why, from a clinical perspective, some patients require targeted therapies as opposed to immunotherapies. *Id.* at ¶¶ 57–62. And during her deposition, Dr. Ortiz-Urda explained that her understanding of how patients would be treated if the Tafinlar–Mekinist combination were unavailable was premised not only on her years of experience and published data, but also on conversations she has had with other physicians outside UCSF. *See* Ortiz-Urda Depo. at 51:17–52:5.

As the Ninth Circuit has acknowledged, "[l]ack of certainty is not, for a qualified expert, the same thing as guesswork." *Primiano*, 598 F.3d at 565. Rather, expert opinion testimony "is reliable if the knowledge underlying it has a reliable basis in the knowledge and experience of the relevant discipline." *Id.* For purposes of this *Daubert* motion, the Court finds that Dr. Ortiz-Urda is qualified and has sufficient expertise in the treatment of metastatic melanoma for her testimony about the treatment of metastatic melanoma to be useful to the jury. She has provided sufficient support for her opinions about what she believes to be the standard of care as well as what treatment options and other considerations a prescriber such as herself would have in the

[2] To the extent Defendant suggests that the Court cannot consider the content of Dr. Ortiz-Urda's expert report in evaluating Defendant's *Daubert* motion, *see* Dkt. No. 243 at 1, that argument is frivolous. The only case Defendant cites, *Hunt v. City of Portland*, 599 F. App'x 620, 621 (9th Cir. 2013), is inapposite. There, the Ninth Circuit concluded that it was error for the district court to admit an expert report at trial because it constituted hearsay to which no hearsay exception applies. Defendant does not cite, and the Court is not aware, of any case that limits the Court's *Daubert* analysis to deposition excerpts.

counterfactual world where the Tafinlar–Mekinist combination was unavailable.

To the extent Defendant disagrees with Dr. Ortiz-Urda's opinions, Defendant may present its own evidence at trial. *See Daubert*, 509 U.S. at 596 ("Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence."). As Defendant's own authority notes, "*Daubert* makes the district court a gatekeeper, not a fact finder." *See United States v. Sandoval-Mendoza*, 472 F.3d 645, 654 (9th Cir. 2006). The jury will ultimately have to decide how persuasive Dr. Ortiz-Urda's counterfactual testimony is. At this stage, the Court finds that Dr. Ortiz-Urda may testify about the standard of care for metastatic melanoma and, based on this, how she thinks that standard of care would change and adapt were the Tafinlar–Mekinist combination no longer available on the market for treating metastatic melanoma.

B. Off Label Prescription Practices for Other Cancers

Second, Dr. Ortiz-Urda opines that if Tafinlar and Mekinist were not available, "physicians would reasonably conclude that the Zelboraf–Cotellic combination would be effective against" cancers for which the Tafinlar–Mekinist combination is approved, but for which the Zelboraf–Cotellic combination is not approved. *See* Ortiz-Urda Report at ¶¶ 69–72. Defendant again contends that Dr. Ortiz-Urda's opinions are speculative and not based on a reliable methodology as she lacks knowledge of how prescribing physicians would behave in this counterfactual world. *See* Dkt. No. 204. In reply, Defendant clarifies that this speculation is particularly acute for Dr. Ortiz-Urda's opinions about off-label use of Zelboraf and Cotellic because Dr. Ortiz-Urda is not an oncologist and does not treat patients for non-small cell lung cancer or anaplastic thyroid cancer. *See* Dkt. No. 243 at 3, 7.

Plaintiff offers little explanation why Dr. Ortiz-Urda should be permitted to testify about physicians' likely behavior when treating cancers other than metastatic melanoma. *See* Dkt. No. 227; *see also* Dkt. No. 341 at 89:15–94:6. Plaintiff instead responds that Dr. Ortiz-Urda's opinion remains reliable because it is premised on the fact that Tafinlar–Mekinist and Zelboraf-Cotellic have "the same mechanism of action." *See* Ortiz-Urda Report at ¶ 72. During her deposition, Dr. Ortiz-Urda further explained that off-label use is more prevalent in the treatment of terminal

diseases where "the patient doesn't have a lot of choices[] and they are running out of time." *See* Ortiz-Urda Depo. at 149:16–150:5. Plaintiff also notes that Defendant's own expert does not challenge Dr. Ortiz-Urda's opinion that off-label use of drugs exists, only its likely frequency in the case of Zelboraf and Cotellic. *See* Dkt. No. 227 at 3.

However, Dr. Ortiz-Urda does not proffer any data on the prevalence or efficacy of the off-label use of Zelboraf or Cotellic, as monotherapies or in combination. To the contrary, she acknowledges that "the prevalence of off-label use focusing on targeted therapies has not been investigated in detail." *See* Ortiz-Urda Report at ¶ 71. Moreover, she acknowledged in her deposition that "[i]t's not true as a general matter that all drugs with the same mechanism of action are clinically equivalent to each other" and "sometimes drugs that have the same mechanism of action may be effective for different indications." *See* Ortiz-Urda Depo. at 149:3-15. In short, Dr. Ortiz-Urda has not provided any facts or data that would raise her opinion about the likelihood of off-label use of Zelboraf and Cotellic beyond a speculative level. And unlike her opinions about the treatment of metastatic melanoma discussed in Section III.A above, her experience cannot fill the gaps here, as she appears to lack any experience in the treatment (off label or otherwise) of non-small cell lung cancer or anaplastic thyroid cancer. As Dr. Ortiz-Urda explains, "[t]he goal of off-label prescribing is to offer a patient an alternative treatment in the absence of a suitable licensed therapy or a lack of clinical trial access." *See* Ortiz-Urda Report at ¶ 71. However, she offers no information about the availability of suitable alternative therapies for other cancers such as non-small cell lung cancer or anaplastic thyroid cancer were Tafinlar and Mekinist unavailable.

Thus, Dr. Ortiz-Urda may not testify about whether and to what extent prescribing physicians would prescribe the Zelboraf–Cotellic combination off label to patients for indications for which Tafinlar–Mekinist is approved but the Zelboraf–Cotellic combination is not.

IV. CONCLUSION

Accordingly, the Court **GRANTS IN PART** and **DENIES IN PART** the motion. Dr. Ortiz-Urda may testify from her own experience about the standard of care for the treatment of metastatic melanoma patients and how she would anticipate patients' treatment changing were Tafinlar and Mekinist not available for metastatic melanoma treatment. However, Dr. Ortiz-Urda

is precluded from offering testimony about whether and to what extent she would anticipate physicians would prescribe the Zelboraf–Cotellic combination for the treatment of any other indications outside metastatic melanoma, including off-label use for the treatment of non-small cell lung cancer and metastatic anaplastic thyroid cancer.

IT IS SO ORDERED.

Dated: 5/26/2020

HAYWOOD S. GILLIAM, JR.
United States District Judge

United States District Court
Northern District of California